United States Department of Health & Human Services
Office of the Secretary
Office of Public Health Emergency Preparedness (OPHEP)

IND Influenza Vaccine: Shortage Program

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Overview

Activities and Challenges

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Overview

- IND Influenza Vaccine: Shortage Program – Activities and Challenges
- IND Vaccine Procurement Process
- FDA Response to Vaccine Shortage
- CDC Plan for Distribution and Administration
- Lessons Learned
- Discussion

Influenza Vaccine Shortage 2004

- **January to August 2004**
  - Manufacturing progressed on schedule with two new strains
  - Anticipated approximately 100 million doses for 2004-2005
- **August 2004**
  - Chiron notified regulatory authorities about sterility issue and investigation to identify cause and implement correction
  - Chiron made a public announcement indicating possible delay in distribution and reduction in vaccine available
- **October 2004**
  - MHRA (the UK regulatory authority) announced suspension of the Chiron license to manufacture inactivated influenza vaccine for 3 months
- **November 2004**
  - Review of situation and consultation between FDA and MHRA and recognition that vaccine planned by Chiron will be unavailable

Activities and Challenges

- **October 11, 2004: HHS Interagency IND Team formed to develop and implement a plan, if necessary, to import influenza vaccines from foreign manufacturers to be used under IND**

- **Composition of IND Team**
  - OS (OPHEP, NVPO, OGC, ASPA, IGA)
  - CDC (NCID, NIP, OGC, PGO, FMO, Emergency Communication System)
  - FDA (CBER,ORA,OCC,OC)
  - CMS
  - HRSA

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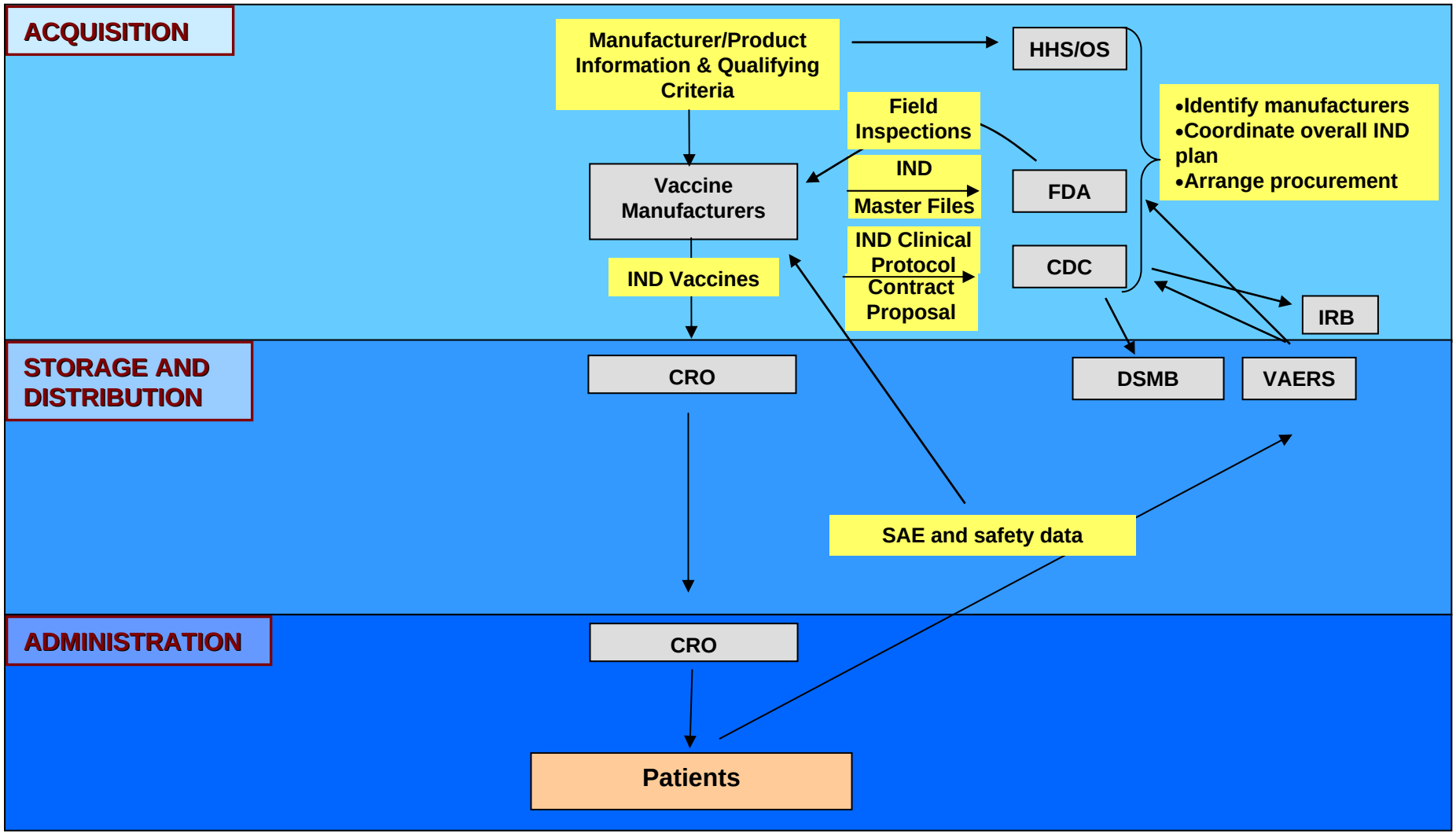
Activities and Challenges

- **Activities**
  - Considered options for availability of investigational products (Investigational New Drug mechanisms,Treatment IND, Emergency Use Authorization)
  - Developed an evolving plan for acquisition, distribution, and administration of foreign influenza vaccine
  - Ensured efficient communication throughout HHS
- **Challenges Encountered**
  - Timing and coordination
  - Purchase of an IND product
  - Coverage and reimbursement issues
  - Decision on sites for administration of IND vaccine / Determining where and when vaccine was needed
  - Modifications to existing systems to accommodate changes needed for IND vaccine administration and monitoring
  - Unknown severity of 2004-05 flu season / changing ACIP recommendations
  - Informing the public and health care professionals on nature of the influenza IND vaccine for shortage use

IND Influenza Vaccine Shortage Program



IND Vaccine Procurement Process

Dr. Robin Robinson
Senior Project Officer
Office of Research and Development Coordination
Office of Public Health Emergency Preparedness
Office of the Secretary

IND Vaccine Procurement Process

- **Inquiry Process**
  - Similar to RFI step in procurement process but in only two weeks
  - 14 international influenza vaccine manufacturing companies were queried by HHS/OS, FDA, and CDC
  - Absolute criteria established by Influenza IND Team
  - Initial questions
    1. Vaccine type, composition, and manufacturing stage
    2. Vaccine availability
    3. Manufacturer's interest (marketing, regulatory, political issues)
    4. Vaccine production capabilities in the future
  - JOFOC established (10/22/04)
  - RFP posted (HHS2005-B-00355) on November 4, 2004.

IND Vaccine Procurement Process

- **Absolute eligibility criteria for selection of vaccine manufacturers for contract consideration**
  - Independent organization, not an agent of a government
  - Licensed influenza vaccine for human use in country of origin
  - Member of WHO's list of pre-qualified vaccine manufacturers **or**
  - Subject to regulatory oversight by the government of countries in FDA's list (Section 802 of FDA Reform and Enhancement Act of 1996 (21 U.S.C. 382)
  - Minimum availability of 500,000 doses of egg-based, trivalent inactivated influenza vaccine
  - Vaccine composition compatible with WHO recommended virus strains for 2004-05 influenza season in Northern Hemisphere
  - Submission of DMF, licensing dossiers and other documents
  - Submission and maintenance of special usage IND application
  - Agreement to CDC IRB approval of IND clinical protocol
  - Permission for FDA field inspections of manufacturing facilities as part of IND acceptance
  - Shipment of vaccine to SNS-designated site through staged shipments no later than January 15, 2005, unless otherwise arranged

IND Vaccine Procurement Process

- Contract was awarded to GSK (12/10/04) for 1.24 M doses of Fluarix influenza vaccine with option to purchase up to 3.4 M doses total
- Contract was awarded to Berna Biotech (1/31/05) for 0.25 M doses of Inflexal V influenza vaccine
- Influenza vaccine was shipped from manufacturers under secure, controlled conditions to vaccine distributor for validated storage
- Limited product liability protection was afforded vaccine manufacturers through VCIP
- Vaccine was inspected and accepted by SNS at vaccine distributor's storage site

FDA Response to Vaccine Shortage

Dr. Norman Baylor
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FDA Response to Vaccine Shortage

- Evaluation of manufacturers for use of unlicensed vaccines under IND
- Inspection of the manufacturing facility for quality of the product – FDA/ORA & CBER.
- Assessment of the chain of custody and storage/transport conditions – FDA/ORA.
- Lot Release by appropriate regulatory authority.

Issue Related to Shortage Use Under IND

- Manufacturer holds IND
- CDC as principal investigator
- Protocol, including safety monitoring
- Product labeling
- Cost recovery

Current FDA Activities to Address the Future

- **Consultation with manufacturers to discuss regulatory mechanisms such as accelerated approval, fast track and priority review to facilitate the path to licensure for new vaccines for the future**

CDC Plans for Distribution and Administration

Dr. Melinda Wharton
Acting Deputy Director
National Immunization Program
Centers for Disease Control and Prevention

CDC IRB as National IRB

- Utilizing CDC's IRB as national IRB for IND protocol
- "Unless precluded by local law or institutional policy, each local site may rely on CDC IRB to meet FDA requirements for IRB review"
- CDC IRB approved protocols, including consent, and patient recruitment messages

Supply of Licensed Vaccine

- **October: Initial distribution of vaccine to existing orders - providers serving high-risk patients**
- **November: States direct vaccine to providers/facilities serving high-risk patients**
- **December: Licensed vaccine continued to be directed to states with ongoing demand in high risk populations**

Vaccine Administration

- **CDC contracted with LHI to provide nationwide access to IND vaccine**
  - Clinic sites
  - Co-PI and other clinic personnel to administer vaccine
- **Administer in accordance with IND protocol**
  - Assure eligibility
  - Obtain informed consent
  - Administer one pre-filled dose IM
  - Enter data into vaccinee database

Informed Consent

- **Informed consent form 4 pages**
- **Revised January 2005 in response to focus group input**
- **Age of consent for IND protocol**
  - Age 14-17 y: vaccinee and parent/guardian signature
  - Age 3-13 y: parent/guardian signature

Inclusion Criteria for Vaccination

- **IND written to include most ACIP-recommended groups, according to January 3 interim recommendations**
- **Children <3 years of age excluded**
  - Practical issue of presentation of GSK IND product
  - Aventis Pasteur filled all pediatric orders; CDC anticipated that supply for this age group would be sufficient
- **Use in pregnant women consistent with product labeling**

Reportable Adverse Events

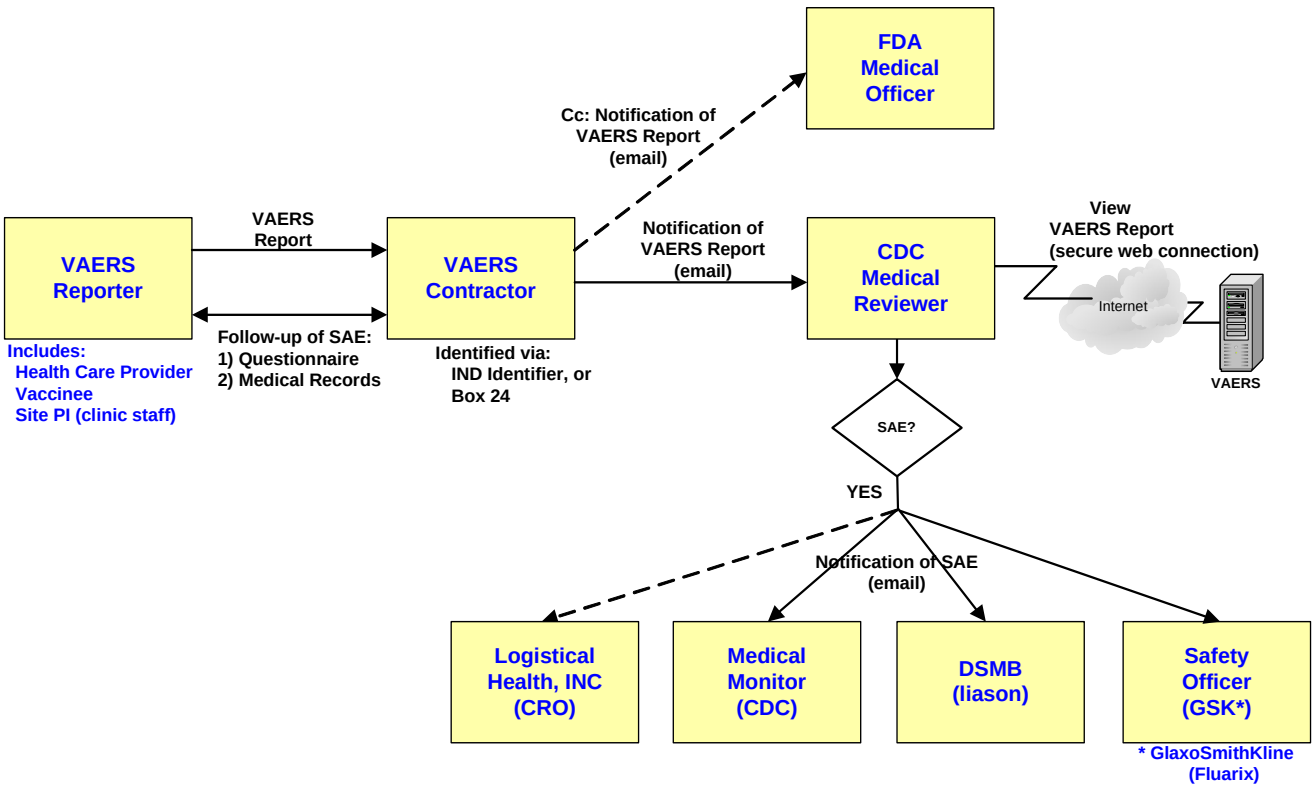
- Serious adverse events
- Allergic reactions
- Vasculitis, with or without renal involvement
- Thrombocytopenia
- Neurologic disorders (encephalomyelitis, neuritis, neuralgia, paresthesia, seizures, Guillain-Barré syndrome)

Adverse Event Surveillance

- VAERS as primary reporting system for adverse events among recipients of IND vaccine
- All vaccinees provided VAERS form pre-printed with vaccine information
- Patient information included instructions for reporting unusual or severe adverse events by mail, on line, or by telephone
- 1-800 numbers for patients and physicians

Adverse Event Surveillance

IND Safety Data Information Flow



Data Safety Monitoring Board

- Composed of 5 persons knowledgeable about immunization
- Review program safety data periodically
- Make recommendations regarding the continuation, modification, or termination of the program
- Render individual expert opinions
- Report to Sponsor and Principal Investigator, who will then report to FDA and CDC IRB

Training for Implementation of IND

- **Preparation of Investigator's Handbook**
- **Training module developed**
  - Administered in person, by webcast, or by conference call
  - Archived on line
- **LHI's Clinician Information Line staff trained on January 14**
- **Additional training planned for LHI clinical staff in 6 clinics in 3-4 states**

Communication Plan for IND Vaccine

- **Special communication challenges for the IND vaccine**
- **Recruitment messages cleared by CDC IRB**
- **Developed template for recruitment materials with space for inclusion of local information.**
- **Recruitment Messages**
  - CDC has acquired more flu vaccine from GSK, Germany. GSK vaccine will help ensure that people at high risk have access to flu vaccine.
  - People should get the vaccine if they are at high risk for serious problems from the flu or are around other people at high risk for serious problems from the flu.

Lessons Learned

- **A model for the use of IND influenza vaccine under shortage conditions was developed. We believe this model is suitable for recurrent use as necessary.**
  - Mechanisms developed to handle coverage, reimbursement, and purchase of IND vaccine
  - Contracts developed for distribution and administration of IND vaccine. These templates are now available for similar situations.
- **Timing**
  - Plan should be in place well ahead of flu season (early summer optimal)
  - Solicitations for manufacturers' proposals drawn up by early summer
  - A thorough distribution plan for utilization of the IND vaccine should be in place by summer
  - Flu vaccine to be used under IND for that year should be shipped no later than October 1

Discussion